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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/06/2002 13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/725,178	MOCKEL ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 21-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 21-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6,10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election without traverse of Group I, Claims 1-7 and 21-23 in Paper No. 12, 2/28/2002, is acknowledged.

Applicants cancellation of the claims of the non elected groups, claims 8-20 is acknowledged. Claims 1-22 are still at issue and are present for examination.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on German Application No. 199 58 160.6, filed December 2, 1999. It is noted that a certified copy of German Application No. 199 58 160.6, has been received

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Applicants filing of information disclosures, paper no. 6, filed 5/21/2001, and paper no. 10, filed 10/12/2001, is acknowledged. Those references considered have been initialed.

Drawings

The drawings filed on 2/9/2000 are accepted and have been approved by the draftsperson.

Specification

The disclosure is objected to because of the following informalities:

On page 1, line 11 of the specification, applicants refer to the "GPM gene". It is suggested that the first time applicants refer to the "GPM gene", this be referred to as the "phosphoglycerate mutase (GPM) gene".

On page 17, applicants list the abbreviations and symbols used throughout the specification, and their corresponding definitions. On line 24 applicants recite "gpm: gpm gene from C. glutamicum" It is suggested that this would also be an appropriate place to write out in full, "phosphoglycerate mutase (GPM) gene".

Appropriate correction is required.

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract of the disclosure is objected to because it appears that applicants have merely copied claim 1 of the instant application to provide the applications' abstract. Further applicants do not recite the polypeptide which is encoded by the taught polynucleotide, other than referring to the gpm gene, and it is not clear if the taught polynucleotide even encodes the gpm gene". As above it is suggested that applicants recite "phosphoglycerate mutase (GPM) gene", such that the abstract can completely describe the taught invention and stand on its own. Further applicants recite "...a polynucleotide **coding** for a polypeptide..." It is suggested that this be amended to "...a polynucleotide which **encodes** for a polypeptide..."

Correction is required. See MPEP § 608.01(b).

Claim Objections

Claims 5-7, 22 and 23 are objected to because of the following informalities:

Claims 6, 22 and 23 each recite "Replicatable...", "Coryneform ..." and "Microorganisms..." respectively. It is suggested that each of Claims 6, 22 and 23 each be amended to recite "The replicatable...", "A coryneform ..." and "The microorganisms..." respectively.

Claims 5 and 7 are objected to because they depend from rejected claim 2.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 and 21-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7 and 21-23 are indefinite in the recitation of "hybridizes" as this term is unclear absent a statement of the conditions under which the hybridization reaction is performed. Nucleic acids which will hybridize under some hybridization conditions will not necessarily hybridize under different conditions. As such it is unclear how homologous to the sequence of a gene encoding SEQ ID NO:2, a sequence must be to be included within the scope of this claim.

Claims 2 and 6 (claims 3, 5 and 7 dependent from) are indefinite in that the recitation "replicatable" is unclear. As any DNA is replicable (i.e. capable of replication) given its insertion in the proper vector and cell environment, it is unclear how this claim further limits claim 1 from which it depends. If it is applicants intent to claim a DNA expression vector which comprises the polynucleotide of claim 1, wherein said expression vector is replicatable in corynebacterium, it is suggested that the claim be amended as such.

Claim 6 is further indefinite in that the recitation "neutral sense mutations in (i)" is unclear. It is not clear what applicants intent is in this part of claim 6. Since in part ii) of claim 6 applicants claim degenerates of SEQ ID NO: 1, applicants must be referring to something other than a degenerate in part iv) of claim 6. Based on this it remains unclear to what applicants consider "neutral sense mutations in (i)" and therefore what is encompassed by this part of the claim.

Claim 22 is indefinite in that it is unclear in applicants recitation, "Coryneform microorganisms..." what applicants intent is. Specifically it is unclear what in addition to microorganisms from the genus Corynebacterium do applicants consider to be a "Coryneform microorganism". Specifically what are the metes and bounds of those microorganisms considered to be encompassed by "Coryneform microorganism". This unclarity is in part based on claim 23 which depends from rejected claim 22, and should further limit claim 22, which recites "Microorganisms according to claim 22 from the genus Corynebacterium. If applicants intent is that "Coryneform microorganism" encompasses those microorganisms from the genus Corynebacterium, only, then claim 23 would be rejected as it would not further limit claim 22.

For similar reasons as discussed above for claim 22, Claim 1 is unclear in the recitation "...polynucleotide from corynebacteria..." Is it applicants intent to claim only those polynucleotides which are in fact isolated from corynebacteria and what do applicants consider to be corynebacteria. Does this mean those polynucleotides isolated from the genus of microorganisms corynebacteria, as discussed above or from a larger genus of microorganisms? Based on the number of claims (i.e. Claims 22 and

23) that depend on Claim 1, discussed above, this recitation is interpreted by the office as not limiting specifically the source of the claimed polynucleotides to the genus corynebacteria.

Claim 22 (Claim 23 dependent from) further recites the limitation "replicatable DNA" of Claims 1 or 6. There is insufficient antecedent basis for this limitation in claim 1.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6, 21-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 21-23 are directed to all possible polynucleotides from corynebacteria which contain a polynucleotide sequence selected from the group consisting of : a) a polynucleotide sequence which is at least 70% identical to a polynucleotide encoding SEQ ID NO: 2, b) a polynucleotide encoding a polypeptide which is at least 80% identical to SEQ ID NO: 2, c) a polynucleotide which is complementary to the polynucleotides of a) or b), and d) a polynucleotide containing at least 15 consecutive bases of a), b) or c) (Claim 1) and a hybridization probe comprising said polynucleotide (Claim 21) and coryneform microorganisms transformed with said

polynucleotides (Claims 22-23). Claims 2-4, 6, 22-23 are directed to all possible polynucleotides according to claim 1 which is a DNA replicatable in corynebacteria (Claim 2), wherein said polynucleotide is a recombinant DNA (Claim 3) or a RNA (Claim 4), wherein said polynucleotide contains at least one sequence is a degenerate of SEQ ID NO: 1 or which hybridizes with the sequence complementary to SEQ ID NO: 1 and coryneform microorganisms transformed with said polynucleotide Claims 6 and 21-23). The specification, however, only provides a single representative species, SEQ ID NO: 1, isolated from *Corynebacteria glutamicum* encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of these polynucleotides by sufficient identifying structural or functional characteristics, for which no predictability is lacking. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-4, 6, 21-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide encoding a polypeptide

which is at least 90% identical to SEQ ID NO: 2, wherein said polypeptide has phosphoglycerate mutase enzymatic activity, does not reasonably provide enablement for any polynucleotide encoding a polypeptide which is at least 70% identical to SEQ ID NO: 2, which hybridizes to a polynucleotide which encodes SEQ ID NO: 2 or comprises at least 15 consecutive bases of SEQ IS NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-5 are so broad as to encompass any polynucleotide encoding a polypeptide which is at least 70% identical to SEQ ID NO: 2, which hybridizes to a polynucleotide which encodes SEQ ID NO: 2 or comprises at least 15 consecutive bases of SEQ IS NO: 1. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims, including all polynucleotides which hybridize to or comprise a mere 15 consecutive bases of SEQ ID NO: 1 wherein said polynucleotides and encoded polypeptides have an undisclosed function/activity. The

claims rejected under this section of U.S.C. 112, first paragraph, place insufficient structural and no functional limits on the claimed polynucleotides. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the polynucleotide having the sequence of SEQ ID NO: 1 and the rejected claims place absolutely no functional limitation on the claimed polynucleotides.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass the modifications and fragments of SEQ ID NO: 1, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting phosphoglycerate mutase enzymatic activity; (B) the general

tolerance of phosphoglycerate mutase enzymes to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a phosphoglycerate mutase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the phosphoglycerate mutase enzymatic activity claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those polynucleotides of the claimed genus having no functional/activity limitation.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including all polynucleotide encoding a polypeptide which is at least 70% identical to SEQ ID NO: 2 and all polynucleotides which hybridize to or comprise a mere 15 consecutive bases of SEQ ID NO: 1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those

skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6 and 21 are rejected under 35 U.S.C. 102(a) as being anticipated by White et al. (Journal of Bacteriology, Vol. 174, No. 2, pages 434-440, January 1992, IDS Reference "TR").

White et al. teach the purification and characterization of the phosphoglycerate mutase enzyme from *Streptomyces coelicolor* and the cloning and sequence analysis of the encoding gene. The polynucleotide taught by White et al. has a best local similarity score of 68.7 % relative to SEQ ID NO: 1, including many regions of higher sequence identity comprising at least 15 contiguous bases of SEQ ID NO: 1. It is acknowledged that the taught polynucleotide of White et al. is not isolated "from corynebacteria", but as discussed above under 112 2nd paragraph rejection, it is believed that this is not a necessary limitation of the claims. Therefore, White et al. anticipate claims 1-4, 6 and 21.

Allowable Subject Matter

Claims 5 and 7 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard Hutson, Ph.D.
Patent Examiner
Art Unit 1652
May 3, 2002